3203556-X-00-01

...e by user-facilities, and manufacturers for ...ATORY reporting.

APPROVED BY FDA ON 03/06/98

Mfr report # 113082

UF/Dist. report #

FDA Use only

...E FDA MEDICAL PRODUCTS REPORTING PROGRAM

A. Patient information

1. Patient identifier: [redacted] In confidence

2. Age at time of event: or 40 YEARS; Date of birth: [redacted]

3. Sex: [X] female [ ] male

4. Weight: 134.9 lbs or 61.2 kgs

B. Adverse event or product problem

1 [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2 Outcomes attributed to adverse event (check all that apply)

[ ] death (mo/day/yr) / /
[ ] life threatening
[X] hospitalization initial or prolonge
[ ] disability
[ ] congenital anomaly
[ ] required intervention to prevent permanent impairment/damage
[ ] other:

3 Date of event (mo/day/yr): AUG / 7 / 1998

4 Date of this report (mo/day/yr): FEB / 15 / 1999

5 Describe event or problem

A 40 YEAR OLD FEMALE PATIENT DEVELOPED HEPATITIS AND RIGHT OVARIAN CYST FOLLOWING THE USE OF VERSED (MIDAZOLAM) FOR SEDATION.

MEDICAL HISTORY INCLUDES HASHIMOTO'S DISEASE WITH HYPOTHYROIDISM, ADDISON'S DISEASE AND FIBROMYALGIA. BLOOD TESTS WERE DONE EVERY 6 MONTHS AND HAD BEEN NORMAL. DECADRON HAD BEEN ADMINISTERED IN THE PAST WITHOUT PROBLEMS. NEVER HAD VERSED BEFORE.
THE PATIENT REPORTS DRUG ALLERGIES TO SULFA, ERYTHROMYCIN AND IODINE. SHE DENIED SMOKING OR ALCOHOL CONSUMPTION.
22 JUL 98: THE PATIENT WAS SCHEDULED TO HAVE A CARTILAGE REPAIR ON HER KNEE.
SODIUM 138 MMOL/L (NORMAL RANGE 137-144), POTASSIUM 3.3 MMOL/L, (NORMAL RANGE 3.5-4.8), CHLORIDE 107 MMOL/L (NORMAL RANGE 101-109), CO2 26 MMOL/L (NORMAL RANGE 24-36), GLUCOSE 95 MG/DL (NORMAL RANGE 78-112), BUN 14 MG/DL (NORMAL RANGE 3-24) AND CREATININE 0.8 MG/DL (NORMAL RANGE 0.6-1.2).
VERSED 3 MG IV, FENTANYL (FLUDROCORTISONE) 100

CONTINUED

6 Relevant tests/laboratory data, including dates

SODIUM
22-JUL-1998
...C RESULT: 138 mmol/L

POTASSIUM
22-JUL-1998

RECEIVED
FEB 18 1999
BY:

CONTINUED

7 Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

ADDISON'S DISEASE
HASHIMOTO'S DISEASE
HYPOTHYROIDISM
DRUG ALLERGY
DRUG ALLERGY
DRUG ALLERGY
FIBROMYALGIA

CONTINUED

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 VERSED INJECTION (MIDAZOLAM HYDROCHLORIDE)
#2 DARVOCET (ACETAMINOPHEN/PROPOXYPHENE NAPSYLATE)

2. Dose, frequency & route
#1 3 MG I per ONE DOSE INTRAVENOUS
#2 ORAL

3. Therapy dates (if unk, give duration) from/to (or best estimate)
#1 22-JUL-1998 / 22-JUL-1998
#2 22-JUL-1998 / 23-JUL-1998

4. Diagnosis for use (indication)
#1 SEDATION
#2 PAIN

5. Event abated after use stopped or dose reduced
#1 [ ] yes [ ] no [X] doesn't apply
#2 [ ] yes [ ] no [X] doesn't apply

6. Lot # (if known)
#1 UNK
#2 UNK

7. Exp. date (if known)
#1 UNK
#2 UNK

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [X] doesn't apply
#2 [ ] yes [ ] no [X] doesn't apply

9. NDC # for product problems only (if known)
#1 NA #2 NA

10. Concomitant medical products and therapy dates (exclude treatment of event)
SYNTHROID CONTINUING
(LEVOTHYROXINE SODIUM)

FLORINEF CONTINUING

CONTINUED

G. All manufacturers

1. Contact Office-name/address

GLOBAL DEVELOPMENT
HOFFMANN-LA ROCHE INC.
340 KINGSLAND STREET
NUTLEY, NJ 07110-1199

2. Phone Number: (973) 562-3523

3. Report source (check all that apply)
[ ] foreign
[ ] study
[ ] literature
[X] consumer
[ ] health professional
[ ] user-facility
[ ] company representive
[ ] distributor
[ ] other:

4. Date received by manufacturer: FEB / 11 / 1999

5 (A)NDA# 18-654
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #: NA

7. Type of report (check all that apply)
[ ] 5-day [X] 15-day
[ ] 10-day [ ] periodic
[ ] initial [X] follow-up # 1

8. Adverse event term(s)
HEPATITIS +++
-RAISED LIVER ENZYMES
-FEELING UNWELL
-RUQ PAIN
-LOSS OF APPETITE
OVARIAN CYST
-LOWER ABDOMINAL PAIN
+++ adverse event that generated submission
- comanifestation

FEB 18 1999

CONTINUED

9 MFR. report number: 113082

E. Initial reporter

1. Name, address & phone #
[redacted]

DSS

CONTINUED

2. Health professional? [ ] yes [X] no

3. Occupation: NURSE

4. Initial reporter also sent report to FDA: [ ] yes [X] unk
FEB 22 1999

FDA 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

ADVERSE EVENT REPORTING SYSTEM

B.5. Describe event or problem - continued

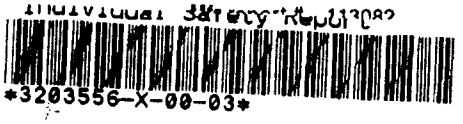
MCG IV, DECADRON (DEXAMTHASONE) 4 MG IM AND 100
MG SOLUCORTEF IV (HYDROCORTISONE SODIUM SUCCINATE) WAS ADMINISTERED. 65 MG SPINAL LIDOCAINE WAS ALSO ADMINISTERED. A PARTIAL MEDIAL MENISCECTOMY WAS COMPLETED WITHOUT ANY PROBLEMS.
THE PATIENT RETURNED HOME WITH DARVOCET N100.
23 JUL 98: THE PATIENT STARTED TO EXPERIENCE A FUZZY SENSATION IN HER HEAD AND STARTED TO EXPERIENCE FLU-LIKE SYMPTOMS SUCH AS HEADACHE, MILD BACKACHE, NAUSEA, WEAKNESS AND HOT FLUSHES. THE CAUSE OF THE HEADACHE WAS THOUGHT TO BE POSSIBLY DUE TO A SUBARACHNOID PUNCTURE.
5 AUG 98: THE PATIENT REPORTED THAT SHE HAD FELT WEAK AND TIRED AND EASILY FATIGUED WITH NAUSEA. SHE WAS ALSO EXPERIENCING SOME URINARY FREQUENCY.
SGOT 235 U/L (NORMAL RANGE 0-33), WBC 11.9 X10^3/UL (NORMAL RANGE 4.5-11). URINE CULTURE SHOWED NO GROWTH.
6 AUG 98: SGOT 149 U/L, SGPT 653 U/L (NORMAL RANGE 0-36), ALK PHOS 82, TOTAL BILIRUBIN 0.7 AND ALBUMIN 4.8 (NORMAL VALUES AND UNITS NOT PROVIDED UNLESS STATED). THERE WAS NO SEROLOGICAL EVIDENCE OF HEPATITIS (A, B OR C). A MONO SPOT TEST WAS POSITIVE. ACETAMINOPHEN LEVEL WAS LESS THAN 1. AN ABDOMINAL ULTRASOUND WAS NORMAL WITH NO ABNORMALITIES OF THE LIVER AND KIDNEYS. THE PATIENT WAS ADMITTED TO HOSPITAL AND IV FLUIDS COMMENCED. ADDISONIAN CRISIS WAS INITIALLY SUSPECTED.
7 AUG 98: THE PATIENT SUDDENLY EXPERIENCED PAIN AND ENLARGEMENT OF HER LIVER. SHE LOST HER APPETITE AND DEVELOPED NAUSEA. SHE ATTENDED ER WHERE BLOOD SAMPLES WERE OBTAINED. LIVER FUNCTION TESTS WERE ELEVATED (VALUES UNSPECIFIED).
12 AUG 98: THE PATIENT WAS EXPERIENCING DISCOMFORT IN THE RIGHT UPPER QUADRANT OF HER ABDOMEN. WBC 13.5 X10^3/UL. SGOT 19 U/L AND SGPT 152 U/L. AN ULTRASOUND OF THE ABDOMEN AND PELVIS WAS PERFORMED REVEALING A COMPLEX MASS IN THE RIGHT ADNEX (SEEN ON PREVIOUS SCANS) WHICH WAS CONSIDERED TO REPRESENT A HAEMORRHAGIC RIGHT OVARIAN CYST OR ENDOMETRIOSIS. THE REMAINDER OF THE PELVIS WAS NORMAL. A FOLLOW-UP SCAN WAS PLANNED FOR 3 MONTHS.
21 AUG 98: THE PATIENT WAS ADMITTED TO HOSPITAL AFTER EXPERIENCING A NEAR SYNCOPAL EPISODE. ELEVATED LIVER ENZYMES STARTED TO DECREASE. DRUG INDUCED HEPATITIS WAS DIAGNOSED, POSSIBLY DUE TO VERSED OR DARVOCET. NO LIVER BIOPSY WAS PERFORMED.
23 AUG 98: THE PATIENT WAS DISCHARGED FROM HOSPITAL. LIVER ENZYME LEVELS WERE WITHIN NORMAL LIMITS.
SHE CONTINUED TO EXPERIENCE PAIN IN THE RIGHT ABDOMINAL AREA WITH WEAKNESS, EXTREME NAUSEA AND A FUZZY SENSATION IN HER HEAD. SHE ALSO SUDDENLY STARTED TO EXPERIENCE A BUZZING SENSATION IN HER HEAD AND PARAESTHESIA AFFECTING HER HANDS AND FOREARMS.
UNKNOWN DATE: THE BUZZING BECAME WORSE, WITH ASSOCIATED INCREASE IN THE SEVERITY OF THE PARAESTHESIA. SHE DEVELOPED INCREASED STOOL FREQUENCY. STOOL CULTURES FOR BACTERIAL ENTERIC PATHOGENS ALONG WITH C.DIFFICILE TOXIN SCREEN WERE ALL NEGATIVE.
3 SEP 98: CYTOMEGALOVIRUS IGM AB WAS NEGATIVE, CMV IGG AB WAS 230 AU/ML, CONSISTENT WITH PAST INFECTION. SGOT 20 U/L, SGPT 26 U/L, WBC 11.3 X10^3/UL.
17 SEP 98: THE PATIENT ATTENDED OUT-PATIENTS FOR FOLLOW-UP. SHE COMPLAINED OF NIGHT SWEATS OVER THE PAST WEEK BUT STATED THAT THEY HAD IMPROVED.
18 SEP 98: A PELVIC ULTRASOUNDWAS PERFORMED REVEALING THE FOLLOWING: THE UTERUS APPEARED NORMALIN SIZE, AND ECHO TEXTURE. NO MYOMETRIAL MASSES WERE NOTED. THE ENDOMETRIAL STRIPE WAS WITHIN NORMAL LIMITS FOR THE PATIENT'S AGE. THE RIGHT OVARY MEASURED 3.8 X 3.5 X 3.78 CM, CONTAINS A CYSTIC STRUCTURE. BASED ON THE REPORT OF THE PREVIOUS ULTRASOUND, THE CYST APPEARED TO HAVE DECREASED IN SIZE. NO SIGNIFICANT INTERNAL ARCHITECTURE OR MATERIAL WAS IDENTIFIED. THE LEFT OVARY APPEARED UNREMARKABLE. IMPRESSION: MOST LIKELY A CYST IN RIGHT OVARY. AN ABDOMINAL ULTRASOUND WAS UNREMARKABLE. THE LIVER APPEARED NORMAL IN SIZE AND ECHOGENICITY.
28 JAN 99: LIVER ENZYME LEVELS WERE NORMAL FOR PAST MONTHS.
THE PATIENT HAD CONSULTED 2 NEUROLOGISTS WHO WERE UNABLE TO MAKE A DIAGNOSIS.
THE BUZZING, PARAESTHESIA AND FUZZY SENSATION WERE PERSISTING.
THE COMPANY CONSIDERED THE HEPATITIS AND THE OVARIAN CYST TO BE MEDICALLY SIGNIFICANT.

B.6. Relevant tests/laboratory data - continued

LAB RESULT: 3.3 mmol/L

CHLORIDE
22-JUL-1998
LAB RESULT: 107 mmol/L

CARBON_DIOXIDE



22-JUL-1998
LAB RESULT: 26 mmol/L

GLUCOSE
22-JUL-1998
LAB RESULT: 95 mg/dL

BLOOD_UREA_NITROGEN
22-JUL-1998
LAB RESULT: 14 mg/dL

CREATININE
22-JUL-1998
LAB RESULT: .8 mg/dL

SGOT
5-AUG-1998
LAB RESULT: 235 U/L

SGOT
6-AUG-1998
LAB RESULT: 149 U/L

SGOT
12-AUG-1998
LAB RESULT: 19 U/L

SGOT
3-SEP-1998
LAB RESULT: 20 U/L

WBC
5-AUG-1998
LAB RESULT: 11.9 x10E3/uL

WBC
12-AUG-1998
LAB RESULT: 13.5 x10E3/uL

WBC
3-SEP-1998
LAB RESULT: 11.3 x10E3/uL

URINE CULTURE
5-AUG-1998

NO GROWTH

SGPT
6-AUG-1998
LAB RESULT: 653 U/L

SGPT
12-AUG-1998
LAB RESULT: 152 U/L

SGPT
3-SEP-1998
LAB RESULT: 26 U/L

HEPATITIS_SCREEN
6-AUG-1998

NEGATIVE

MONOSPOT_TEST
6-AUG-1998

POSITIVE

ALK_PHOSPHATASE
6-AUG-1998
LAB RESULT: 82

NO NORMAL VALUES OR UNITS PROVIDED.

BILIRUBIN_TOTAL
6-AUG-1998
LAB RESULT: .7

NO NORMAL VALUES OR UNITS PROVIDED.

ALBUMIN
6-AUG-1998
LAB RESULT: 4.8

NO UNITS OR NORMAL VALUES PROVIDED.

STOOL_CULTURE

NEGATIVE

ULTRASOUND SCAN
12-AUG-1998

AN ULTRASOUND OF THE ABDOMEN AND PELVIS WAS PERFORMED REVEALING A COMPLEX MASS IN THE RIGHT ADNEX (SEEN ON PREVIOUS SCANS) WHICH WAS CONSIDERED TO REPRESENT A HAEMORRHAGIC RIGHT OVARIAN CYST OR ENDOMETRIOSIS. THE REMAINDER OF THE PELVIS WAS NORMAL.

ULTRASOUND SCAN
18-SEP-1998

A PELVIC ULTRASOUND WAS PERFORMED REVEALING THE FOLLOWING: THE UTERUS APPEARED NORMAL IN SIZE, AND ECHO TEXTURE. NO MYOMETRIAL MASSES WERE NOTED. THE ENDOMETRIAL STRIPE WAS WITHIN NORMAL LIMITS FOR THE PATIENT'S AGE. THE RIGHT OVARY MEASURED 3.8 X 3.5 X 3.78 CM. BASED ON THE REPORT OF THE PREVIOUS ULTRASOUND, THE CYST APPEARED TO HAVE DECREASED IN SIZE. NO SIGNIFICANT INTERNAL ARCHITECTURE OR MATERIAL WAS IDENTIFIED. THE LEFT OVARY APPEARED UNREMARKABLE.

ULTRASOUND SCAN
18-SEP-1998

AN ABDOMINAL ULTRASOUND WAS UNREMARKABLE. THE LIVER APPEARED NORMAL IN SIZE AND ECHOGENICITY.

DRUG_LEVEL
6-AUG-1998

ACETAMINOPHEN LEVEL LESS THAN 1.

B.7. Other relevant history - continued

THE PATIENT DOES NOT SMOKE OR DRINK.

C.10. Concomitant medical products and Therapy Dates - continued

(FLUDROCORTISONE ACETATE)

ELAVIL CONTINUING
(AMITRIPTYLINE HYDROCHLORIDE)

Individual Safety Report

3203556-X-00-05

TYLENOL UNK
(ACETAMINOPHEN)

FENTANYL 22-JUL-1998 / 22-JUL-19S
(FENTANYL CITRATE)

DECADRON 22-JUL-1998 / 22-JUL-1998
(DEXAMETHASONE)

SOLU-CORTEF 22-JUL-1998 / 22-JUL-1998
(HYDROCORTISONE SODIUM SUCCINATE)

LIDOCAINE 22-JUL-1998 / 22-JUL-1998
(LIDOCAINE)

PREDNISONE CONTINUING
(PREDNISONE)

E.1. Initial reporter (Name, address & phone #) - continued

[redacted]

UNITED STATES OF AMERICA

G.8. Adverse event term(s) - continued

BACKACHE
TINNITUS
INCREASED URINARY FREQUENCY
RAISED WBC
FLUSHING
HEADACHE
WEAKNESS
NAUSEA
PARAESTHESIA
DIZZINESS
LAB TEST ABNORMAL
INCREASED STOOL FREQUENCY